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(12) **United States Patent**
Yock et al.(10) Patent No.: **US 6,346,098 B1**(45) Date of Patent: **Feb. 12, 2002**(54) **METHODS AND KITS FOR LOCALLY
ADMINISTERING AN ACTIVE AGENT TO
AN INTERSTITIAL SPACE OF A HOST**(75) Inventors: **Paul G. Yock; Ali H. Hassan; Alan
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CA (US)**(*) Notice: Subject to any disclaimer, the term of this
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U.S.C. 154(b) by 0 days.(21) Appl. No.: **09/519,950**(22) Filed: **Mar. 7, 2000**(51) Int. Cl.⁷ **A61M 25/00; A61K 38/00;
A61K 48/00; A61K 31/715**(52) U.S. Cl. **604/508; 604/507; 514/2;
514/44; 514/54**(58) Field of Search **514/2, 44, 54;
604/96.01, 508, 509, 510, 507; 607/1; 11/11**(56) **References Cited****U.S. PATENT DOCUMENTS**

4,459,977 A	7/1984	Pizon et al.	600/17
4,689,041 A	8/1987	Corday et al.	604/509
4,934,996 A	6/1990	Mohl et al.	600/17
5,011,468 A	4/1991	Lundquist et al.	600/18
5,533,957 A	7/1996	Aldea	600/16
5,597,377 A	1/1997	Aldea	600/16
5,824,071 A	10/1998	Nelson et al.	606/194
5,874,402 A	* 2/1999	Singh et al.	514/2
5,885,238 A	3/1999	Stevens et al.	604/6.14
5,913,842 A	6/1999	Boyd et al.	604/28
5,922,687 A	7/1999	Mann et al.	514/44
5,925,683 A	7/1999	Park	514/772.1
5,985,847 A	11/1999	Carson et al.	514/44

OTHER PUBLICATIONS

Baumbach et al. (1999). "Local drug delivery: Impact of pressure, substance characteristics, and stenting on drug transfer into the arterial wall" *Catheterization and Cardiovascular Interventions*, vol. 47: 102-106.

Boekstegers et al. (1999). "Regional and highly efficient myocardial gene transfer by selective pressure-regulated retroinfusion of coronary veins" *JACC, Abstracts, Hypertension, Vascular Disease, and Prevention* p.223A.

Boekstegers et al. (1998). "Selective suction and pressure-regulated retroinfusion: An effective and safe approach to retrograde protection against myocardial Ischemia in patients undergoing normal and high risk percutaneous transluminal coronary angioplasty" *JACC*, vol. 31(7): 1525-1533.

Boekstegers et al. (2000). "Myocardial gene transfer by selective pressure-regulated retroinfusion of coronary veins" *Gene Therapy*, vol. 7:232-240.

Gerber et al. (2000). "The coronary venous system: An alternate portal to the myocardium for diagnostic and therapeutic procedures in invasive cardiology" *Current Interventional Cardiology Reports*, vol. 2: 27-37.

Von der Leyen et al. (1999). "A pressure-mediated nonviral method for efficient arterial gene and oligonucleotide transfer" *Human Gene Therapy*, vol. 10: 2355-2364.

* cited by examiner

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(57) **ABSTRACT**

Methods are provided for locally administering an agent to a host. Specifically, the subject methods provide for the local administration of an agent to an interstitial space of a host. In the subject methods, an agent is retroinfused into a vessel of a host, typically a vein, under conditions sufficient for the agent to enter an interstitial space of the host proximal to the vessel location into which the agent is retroinfused. In practicing the subject methods, the agent is administered to the host in combination with the production of vascular stress at the site of administration, where the vascular tissue stress is sufficient to provide for transport of the agent from the vascular site of deposition into the target interstitial space. In a preferred embodiment, the agent is retroinfused at a pressure sufficient to provide for mechanical stress on the vessel proximal to the target interstitial space. Also provided are kits for use in practicing the subject methods. The subject invention finds use in the local administration of a variety of different agents for treatment of a variety of different disease or other conditions.

19 Claims, 2 Drawing Sheets